

Substitute for Form 1449/A/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet 1 of 9

Complete if Known

Application No.	09/780,650
Filing Date	02/12/2001
First Named Inventor	D'Amato
Group Art Unit	1616
Examiner Name	Badio, B.
Attorney Docket Number	05213-0493 (43170-253692)

U.S. PATENT DOCUMENTS

Examiner Initials	Cite No. ¹	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number ⁴	Kind Code ³ (if known)			
DD	1	4,172,132		Draper et al.	10/23/1979	
	2	4,522,758		Ward et al.	06/11/1985	
	3	4,743,597		Javitt et al.	05/10/1988	
	4	5,001,116		Folkman et al.	03/19/1991	
	5	5,504,074		D'Amato et al.	04/02/1996	
DD	6	5,643,900		Fotsis et al.	07/01/1997	

Examiner Signature	Badio	Date Considered	1/23/03
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Sheet	2	of	9				
FOREIGN PATENT DOCUMENTS							
Examiner Initials	Cite No. ¹	Foreign Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T*
		Office ³	Number ⁴				
BB	7	WO	90/15816	A1	The UpJohn Company	12/27/1990	
BB	8	WO	93/03729		Research Corporation Technologies, Inc.	03/04/1993	

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BB	9	Author: Title: Publ: Research Plus Catalog Vol/Iss: Pages: 50-58 Date: 1993			
	10	Author: Title: U.S. Patent Application No. 09/641,327 filed August 18, 2000 entitled "Antiangiogenic Agents" Publ: Vol/Iss: Pages: Date:			
	11	Author: Title: U.S. Patent Application No. 09/779,331 filed February 8, 2001 entitled "Antiangiogenic Agents" Publ: Vol/Iss: Pages: Date:			
	12	Author: Title: U.S. Patent Application No. 10/077,142 filed February 15, 2002 entitled "Estrogenic Compounds as Anti-Mitotic Agents" Publ: Vol/Iss: Pages: Date:			
	13	Author: Title: U.S. Patent Application No. 09/866,279 filed May 25, 2001 entitled "Use of Estrogenic Compounds as Anti-Fungal Agents" Publ: Vol/Iss: Pages: Date:			
	14	Author: Title: U.S. Patent Application No. 09/899,702 filed July 5, 2001 entitled "Estrogenic Compounds as Antiangiogenic Agents" Publ: Vol/Iss: Pages: Date:			
BB	15	Author: Title: U.S. Patent Application No. 09/939,208 filed August 24, 2001 entitled "Antiangiogenic Agents" Publ: Vol/Iss: Pages: Date:			

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722	16	Author: ADAMS, E.F. et al. Title: Steroidal regulation of oestradiol-17B dehydrogenase activity of the human breast cancer cell line MCF-7 (Chemical Abstracts Doc. No. 109:32325, 1988) Publ: Journal of Endocrinology Vol/Iss: 188 (1) Pages: 149-154 Date: 07/1988			
	17	Author: BHAT et al. Title: Estradiol-induced Mitotic Inhibition in the Bursa of Fabricius of Male Domestic Duckling (Chemical Abstracts Doc. No: 98:31837, 1982) Publ: Mikroskopie Vol/Iss: 39 Pages: 113-117 Date: 05/1982			
	18	Author: BLICKENSTAFF et al. Title: Estrogen-Catharanthus (Vinca) Alkaloid Conjugates (Chemical Abstracts Doc. No: 94:114277, 1981) Publ: Cytotoxic Estrogens in Hormone Receptive Tumors Vol/Iss: Pages: 89-105 Date: 1980			
	19	Author: BOYE et al. Title: 185. Deaminocolchinyll Methyl Ether: Synthesis from 2,3,4,4'-Tetramethoxybiphenyl -2-carbaldehyde. Comparison of Antitubulin Effects of Deaminocolchinyll Publ: Helvetica Chimica Acta Vol/Iss: 72 Pages: 1690-1696 Date: 1989			
	20	Author: CRUM, R. et al. Title: A New Class of Steroids Inhibits Angiogenesis in the Presence of Heparin or a Heparin Fragment Publ: SCIENCE Vol/Iss: 230 Pages: 1375-1378 Date: 12/20/85			
	21	Author: EVANS et al. Title: A Convergent Total Synthesis of (+)- Colchicine and (+)- Desacetamidisocolchicine Publ: Journal of the American Chemical Society Vol/Iss: 103 Pages: 5813-5821 Date: 09/23/81			
722	22	Author: FITZGERALD Title: Molecular Features of Colchicine Associated with Antimitotic Activity and Inhibition of Tubulin Polymerization Publ: Biochemical Pharmacology Vol/Iss: 25 Pages: 1383-1387 Date: 06/15/76			

Examiner Signature	Badio	Date Considered	1/24/03
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				Group Art Unit	1616
				Examiner Name	Badio, B.
Sheet	6	of	9	Attorney Docket Number	05213-0493 (43170-25862)
OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS					
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BB	30	Author: MORGAN et al. Title: Calcium and Oestrogen Interactions upon the Rat Thymic Lymphocyte Plasma Membrane (Chemical Abstracts Doc. No: 85:172052, 1976) Publ: Biochemical and Biophysical Research Communications Vol/Iss: 72 (2) Pages: 663-672 Date: 09/20/76			
	31	Author: MUKUNDAN et al. Title: Liver Regeneration in Oral Contraceptive Treated Female Rats - Effects of Moderate Malnutrition (Chemical Abstracts Doc. No: 102:143342, 1984) Publ: Hormone and Metabolic Research Vol/Iss: 16 (12) Pages: 641-645 Date: 12/1984			
	32	Author: NAKAMURA et al. Title: Studies on the Total Synthesis of <i>dl</i> -Colchicine. I. Synthesis of 3-Hydroxy-9, 10, 11-trimethoxy-1,2,3,4,6,7-hexahydro-5H-dibenzo[a,c] cycloheptatrien-5-one Publ: Chemical and Pharmaceutical Bulletin Vol/Iss: 10 Pages: 281-290 Date: 1962			
	33	Author: OPPOLZER et al. Title: 177. The Enantioselective Synthesis of (+)-Estradiol from 1,3-Dihydrobenzo[c] thiophene-2,2-dioxide by Successive Thermal SO ₂ -Extrusion and Cycloaddition Reactions Publ: Helvetica Chimica Acta Vol/Iss: 63 Pages: 1703-1707 Date: 1980			
	34	Author: PAULL et al. Title: Identification of Novel Antimitotic Agents Acting at the Tubulin Level by Computer-assisted Evaluation of Differential Cytotoxicity Data Publ: Cancer Research Vol/Iss: 52 Pages: 3892-3900 Date: 07/15/92			
	35	Author: POLI et al. Title: Tumor Necrosis Factor α Functions in an Autocrine Manner in the Induction of Human Immunodeficiency Virus Expression Publ: Proceedings of the National Academy of Science USA Vol/Iss: 87 Pages: 782-785 Date: 01/1990			
BB	36	Author: RAO et al. Title: Structural Specificity of Estrogens in the Induction of Mitotic Chromatid Non-Disjunction in Hela Cells Publ: Experimental Cell Research Vol/Iss: 48 Pages: 71-81 Date: 1967			

Examiner Signature	<i>Badio</i>	Date Considered	1/24/03
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				Group Art Unit	1616	
Examiner Name	Badio, B.					
Attorney Docket Number	05213-0493 (43170-251692)					
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OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS						
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BB	23	Author: GETAHUN et al. Title: Synthesis of Alkoxy-Substituted Diaryl Compounds and Correlation of Ring Separation with Inhibition of Tubulin Polymerization: Differential Enhancement of Inhibitory Effects Under Suboptimal Polymerization Reaction Conditions Publ: Journal of Medical Chemistry Vol/Iss: 35 (6) Pages: 1058-1067 Date: 03/20/92				
	24	Author: GROSS et al. Title: Inhibition of Tumor Growth, Vascularization, and Collagenolysis in the Rabbit Cornea by Medroxyprogesterone Publ: Proceedings of the National Academy of Science USA Vol/Iss: 78 (2) Pages: 1176-1180 Date: 02/1981				
	25	Author: HARTLEY-ASP et al. Title: Diethylstilbestrol Induces Metaphase Arrest and Inhibits Microtubule Assembly Publ: Mutation Research Vol/Iss: 143 (4) Pages: 231-235 Date: 08/1985				
	26	Author: HUBER et al. Title: Tubulin Binding of Conformationally Restricted Bis-Aryl Compounds Publ: Bioorganic & Medicinal Chemistry Letters Vol/Iss: 1 (5) Pages: 243-246 Date: 1991				
	27	Author: LIN et al. Title: Interactions of Tubulin with Potent Natural and Synthetic Analogs of the Antimitotic Agent Combretastatin: A Structure-Activity Study Publ: Molecular Pharmacology Vol/Iss: 34 (2) Pages: 200-208 Date: 08/1988				
28	Author: LINCOLN et al. Title: Conformation of Thiocolchicine and Two B-Ring-Modified Analogues Bound to Tubulin Studied with Optical Spectroscopy Publ: Biochemistry Vol/Iss: 30 (5) Pages: 1179-1187 Date: 02/05/91					
BB	29	Author: LOTTERING et al. Title: Effects of the 17 β -Estradiol Metabolites on Cell Cycle Events in MCF-7 Cells (Chemical Abstracts Doc. No: 117:245769, 1992) Publ: Cancer Research Vol/Iss: 52 Pages: 5926-5932 Date: 11/01/92				

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First Named Inventor

D'Amato

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37

Author: RAVINDRA, R.

Title: Effect of Estradiol on the *in vitro* Assembly of Rat Brain Tubulin

Publ:

Journal of Indian Institute of Science

Vol/Iss: 64 (3)

Pages: 27-35

Date: 03/1983

38

Author: SAKAKIBARA et al.

Title: Effects of Diethylstilbestrol and its Methyl Ethers on Aneuploidy Induction and Microtubule Distribution in Chinese Hamster V79 cells

Publ:

Mutation Research

Vol/Iss: 263

Pages: 269-276

Date: 08/1991

39

Author: SATO et al.

Title: Effect of Estradiol and Ethynylestradiol on Microtubule Distribution in Chinese Hamster V79 Cells

Publ:

Chemical and Pharmaceutical Bulletin

Vol/Iss: 40 (1)

Pages: 182-184

Date: 01/1992

40

Author: SATO et al.

Title: Disruptive Effect of Diethylstilbestrol on Microtubules

Publ:

Gann

Vol/Iss: 75

Pages: 1046-1048

Date: 12/1984

41

Author: SAWADA et al.

Title: Colchicine-Like Effect of Diethylstilbestrol (DES) on Mammalian Cells in Vitro

Publ:

Mutation Research

Vol/Iss: 57

Pages: 175-182

Date: 05/1978

42

Author: SEEGERs et al.

Title: Cyclic-AMP and Cyclic-GMP Production in MCF-7 Cells Exposed to Estradiol-17 Beta, Catecholestrogens and Methoxy-Estrogens in MCF-7 Cells (Meeting Abstract only)

Publ:

Joint MCI-1st Symposium. Third 1st International Symposium. Biology and Therapy of Breast Cancer

Vol/Iss:

Pages:

Date: 09/25/89

43

Author: SEEGERs, J.C. et al.

Title: The Cytotoxic Effects of Estradiol-17B, Catecholestrogens and Methoxyestradiols on Dividing MCF-7 and HeLa Cells

Publ:

Journal of Steroid Biochemistry

Vol/Iss: 32 (6)

Pages: 797-809

Date: 1989

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BB	44	Author: SHARP et al. Title: Diethylstilbestrol: the Binding and Effects of Diethylstilboestrol upon the Polymerisation and Depolymerisation of Purified Microtubule Protein in vitro Publ: Carcinogens Vol/Iss: 6 (6) Pages: 865-871 Date: 06/1985			
	45	Author: SPICER et al. Title: Catecholestrogens Inhibit Proliferation and DNA Synthesis of Porcine Granulosa Cells in Vitro: Comparison with Estradiol, 5 α -dihydrotestosterone, Gonadotropins and Catecholamines (Chemical Abstracts Doc. No: Publ: Molecular and Cellular Endocrinology Vol/Iss: 64 Pages: 119-126 Date: 1989			
	46	Author: STERNLICHT et al. Title: Colchicine Inhibition of Microtubule Assembly via Copolymer Formation Publ: The Journal of Biological Chemistry Vol/Iss: 254 (20) Pages: 10540-10550 Date: 10/25/79			
	47	Author: SUN et al. Title: Antitumor Agents. 139. Synthesis and Biological Evaluation of Thiocolchicine Analogs 5,6-Dihydro-6(S)-(acyloxy)-and 5,6-Dihydro-6(S)-[(acyloxy)methyl]-1,2,3-trimethoxy-9-(methylthio)-8H-cyclohepta[a]naphthalene-8-ones as Novel Cytotoxic Publ: Journal of Medicinal Chemistry Vol/Iss: 36 Pages: 544-551 Date: 03/05/93			
	48	Author: SUNAGAWA et al. Title: Synthesis of Colchicine; Synthesis of <i>d,l</i> -'Demethoxydeoxy-hexahydrocolchicine Publ: Chemical & Pharmaceutical Bulletin Vol/Iss: 9 Pages: 81-83 Date: 1961			
	49	Author: TSUTSUI et al. Title: Comparison of Human Versus Syrian Hamster Cells in Culture for Induction of Mitotic Inhibition, Binucleation and Multinucleation, Following Treatment with Four Aneuploidogens Publ: Toxicology in Vitro Vol/Iss: 4 (1) Pages: 75-84 Date: 1990			
BB	50	Author: VAN TAMELEN et al. Title: The Synthesis of Colchicine Publ: Tetrahedron Vol/Iss: 14 Pages: 8-34 Date: 09/1961			

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BB	51	Author: WHEELER et al. Title: Mitotic Inhibition and Aneuploidy Induction by Naturally Occurring and Synthetic Estrogens in Chinese Hamster Cells in Vitro Publ: Mutation Research Vol/Iss: 171 Pages: 31-41 Date: 1986			
BB	52	Author: WHEELER et al. Title: Mitotic Inhibition and Chromosome Displacement Induced by Estradiol in Chinese Hamsters Cells (Chemical Abstracts Doc. No: 105:54822, 1986) Publ: Cell Motility and the Cytoskeleton Vol/Iss: 7 (3) Pages: 235-247 Date: 1987			

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